

APPLICANT FACSIMILE OF FORM PTO-1449
 REV 7-80

 U.S. DEPARTMENT OF COMMERCE
 PATENT AND TRADEMARK OFFICE

ATTY DOCKET NO.

SERIAL NO.

BBI-013C3CN3

09/777317

APPLICANT

Bujard, H. et al.

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U.S. PATENT DOCUMENTS

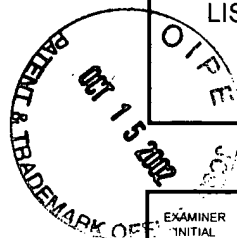
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
RR	AA	5,464,758	11/95	Gossen et al.	435	69.1	
	AB	5,221,778	6/93	Byrne et al.	800	2	
	AC	5,545,808	8/96	Hew et al.	800	2	
	AD	5,595,895	1/97	Miki et al.	435	172.3	
RR	AE	4,833,080	5/89	Brent et al.	435	172.3	

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
RR	AF	WO 96/01313	01/96	PCT			
	AG	WO 94/29442	12/94	PCT			
	AH	WO 94/18317	08/94	PCT			
	AI	WO 94/04672	03/94	PCT			
	AJ	WO 93/23431	11/93	PCT			
	AK	WO 93/04169	03/93	PCT			
	AL	WO 92/20808	11/92	PCT			
	AM	WO 92/11874	07/92	PCT			
	AN	0 494 724 A2	07/92	EPO			
	AO	WO 91/19796	12/91	PCT			
	AP	WO 91/19784	12/91	PCT			
	AQ	WO 91/13979	9/91	PCT			
	AR	0 455 687 B1	11/91	EPO			
	AS	0 455 424 A2	11/91	EPO			
RR	AT	EP 0 332 416	09/89	EPO			

OTHERS (including Author, Title, Date, Pertinent Pages, Etc.)

RR	AU	Ackland-Berglund, C.E. and Leib, D.A. (1995) <i>BioTechniques</i> 19:216-217
RR	AV	Ackland-Berglund, C.E. and Leib, D.A. (1995) "Efficacy of Tetracycline-Controlled Gene Expression Is Influenced by Cell Type" <i>BioTechniques</i> 18(2):196-200
Examiner		RR
Date Considered		5/30/03
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BA	Agarwal, M.L. et al. (1995) "p53 Controls Both the G ₂ /M and the G ₁ Cell Cycle Checkpoints and Mediates Reversible Growth Arrest in Human fibroblasts," <i>Proceedings of the National Academy of Science, Sci. USA</i> , 92:8493-8497
BB	Altschmied, L. et al. (1988) "A threonine to alanine exchange at position 40 of Tet repressor alters the recognition of the sixth base pair of tet operator from GC to AT", <i>The EMBO Journal</i> , 7(12):4011-4017
BC	Baim, S.B. et al. (1991) "A chimeric mammalian transactivator based on the lac repressor that is regulated by temperature and isopropyl β -D-thiogalactopyranoside", <i>Proceedings of the National Academy of Science</i> 88: 5072-5076
BD	Baniahmad, A. et al. (1992) "A Transferable Silencing Domain Is Present In the Thyroid Hormone Receptor, In the v-erbA Oncogene Product and In the Retinoic Acid Receptor" <i>The EMBO Journal</i> 11(3):1015-1023
BE	Baumeister, R. et al. (1992) "Tet Repressor Tet Operator Interactions Derived From Mutants With New Recognition Specificities", <i>Structural Tools For The Analysis Of Protein-Nucleic Acid Complexes Advances In Life Sciences</i> , Birkhauser, Basel ;Boston, pp. 175-183
BF	Baumeister, R. et al. (1992) "Contacts Between Tet Repressor And Tet Operator Revealed By New Recognition Specificities Of Single Amino Acids Replacement Mutants", <i>Journal Of Molecular Biology</i> , 226:1257-1270
BG	Baumeister, R. et al. (1992) "Functional Roles Of Amino Acid Residues Involved In Forming THE Alpha-helix-turn-alpha-helix operator DNA Binding Motif Of Tet repressor From Tn10", <i>Proteins: Structure, Function, and Genetics</i> , 14(2):168-177
BH	Bergman, M. et al. (1995) "Overexpressed Csk Tyrosine Kinase Is Localized in Focal Adhesions, Causes Reorganization of $\alpha_v\beta_5$ Integrin, and Interferes with HeLa Cell Spreading", <i>Molecular and Cellular Biology</i> , 15(2):711-722
BI	Boshart, M. et al. (1985) "A Very Strong Enhancer Is Located Upstream of an Immediate Early Gene of Human Cytomegalovirus", <i>Cell</i> 41(2):521-530
BJ	Bradley, A. (1991) "Modifying the mammalian genome by gene targeting", <i>Current Opinion in Biotechnology</i> 2: 832-829
BK	Bradley, A. (1992) "Modifying The Mouse: Design And Desire", <i>Biotechnology</i> , 10: 534-539
BL	Brent, R. and M. Ptashne (1984) "A Bacterial Repressor Protein or a Yeast Transcriptional Terminator Can Block Upstream Activation of A Yeast Gene" <i>Nature</i> 312:612-615
BM	Brent R. and M. Ptashne (1985) "A Eukaryotic Transcriptional Activator Bearing the DNA Specificity of a Prokaryotic Repressor" <i>Cell</i> 43:729-736
BN	Brown, M., et al. (1987) "lac Repressor Can Regulate Expression from a Hybrid SV40 Early Promoter Containing a lac Operator in Animal Cells", <i>Cell</i> . 49:603-612
BO	Buckbinder L. et al. (1994) "Gene Regulation by Temperature-Sensitive p53 Mutants: Identification of p53 response genes" <i>Proc. Natl. Acad. Sci. USA</i> 91:10640-10644
BP	Capecchi, M.R. (1989) "Altering the Genome by Homologous Recombination", <i>Science</i> 244:1288-1292

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CA	Cayrol, C. et al. (1995) "Identification of Cellular Target Genes of the Epstein-Barr Virus Transactivator Zta: Activation of Transforming Growth Factor β h3 (TGF- β h3) and TGF- β 1", <i>Journal of Virology</i> , 69(7):4206-4212
CB	Chen, Y.Q. et al. (1995) "Tumor Suppression by p21 ^{WAF1} ", <i>Cancer Research</i> , 55:4536-4539
CC	Coghlan, A. (1995) "Gene dream fades away" <i>New Scientist</i> 148:14-15
CD	Courey, A.J. and Tjian, R., (1988) "Analysis of Sp1 In Vivo Reveals Multiple Transcriptional Domains, Including a Novel Glutamine-Rich Activation Motif", <i>Cell</i> 55:887-898
CE	Cowell, (1994) "Repression versus activation in the control of gene transcription," <i>Trends in Biochemical Sciences</i> , 19:1, 38-42
CF	Crystal, R.G. (1995) "Transfer of Genes to Humans: Early Lessons and Obstacles to Success", <i>Science</i> 270: 404-410
CG	Daddona et al. (1984) "Human Adenosine Deaminase." <i>J. Biol. Chem.</i> 259: 12101-12106
CH	Damke, H. et al. (1994) "Induction of Mutant Dynamin Specifically Blocks Endocytic Coated Vesicle Formation." <i>The Journal of Cell Biology</i> 127 (4): 915-934
CI	Damke, H. et al. (1995) "Tightly Regulated and Inducible Expression of Dominant Interfering Dynamin Mutant in Stably Transformed HeLa Cells." <i>Methods in Enzymology</i> 257: 209-220
CJ	Degenkolb, J. et al. (1991) "Structural Requirements of Tetracycline-Tet Repressor Interaction: Determination of Equilibrium Binding Constants for Tetracycline Analogs with the Tet Repressor" <i>Antimicrobial Agents and Chemotherapy</i> 35(8):1591-1595
CK	Deuschle, U., et al. (1989) "Regulated expression of foreign genes in mammalian cells under the control of coliphage T3 RNA polymerase and lac repressor", <i>Proceedings of the National Academy of Science USA</i> 86:5400-5404
CL	Deuschle et al. (1995) "Tetracycline-reversible silencing of eukaryotic promoters," <i>Mol. Cell. Biol.</i> , 15:4, 1907-1914
CM	Dhawan, J. et al. (1995) "Tetracycline-Regulated Gene Expression Following Direct Gene Transfer into Mouse Skeletal Muscle", <i>Somatic Cell and Molecular Genetics</i> , 21(4):233-240
CN	Ebert, K.M. et al. (1988) "A Moloney MLV-Rat Somatotropin Fusion Gene Produces Biologically Active Somatotropin in a Transgenic Pig." <i>Molecular Endocrinology</i> 2(3): 277-283
CO	Efrat, S. et al. (1995) "Conditional Transformation of a Pancreatic β -Cell Line Derived From Transgenic Mice Expressing A Tetracycline-Regulated Oncogene" <i>PNAS. USA</i> , 92:3576-3580
CP	Englert, C. et al. (1995) "WT1 suppresses synthesis of the epidermal growth factor receptor and induces apoptosis," <i>EMBO journal</i> , 14(19):4662-4675
CQ	Epstein-Baak, R. et al. (1992) "Inducible Transformation of Cells from Transgenic Mice Expressing SV40 under Lac Operon Control", <i>Cell Growth & Differentiation</i> 3:127-134
CR	Fieck, A. et al. (1992) "Modifications of the <i>E. Coli</i> Lac Repressor for Expression in Eukaryotic Cells: Effect of Nuclear Signal Sequence on Protein Activity and Nuclear Documentation", <i>Nucleic Acids Research</i> 20:1785-1791

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DA	Fields, S. et al. (1989) "A novel genetic system to detect protein-protein interactions" <i>Nature</i> 340: 245-246
DB	Figge, J., et al. (1988) "Stringent Regulation of Stably Integrated Chloramphenicol Acetyl Transferase Genes by <i>E. coli lac</i> Repressor in Monkey Cells", <i>Cell</i> 52:713-722
DC	Fishman G. et al. (1994) "Tetracycline-Regulated Cardiac Gene Expression in Vivo" <i>J. Clin. Invest.</i> 93:1864-1868
DD	Frankel, F.D. et al. (1988) "Tat Protein from Human Immunodeficiency Virus Forms a Metal-Linked Dimer" <i>Science</i> 240: 70-73
DE	Früh, K. et al. (1994) "Displacement of Housekeeping Proteasome Subunits by MHC-encoded LMP's: a Newly Discovered Mechanism for Modulating the Multicatalytic Proteinase Complex." <i>EMBO Journal</i> 13 (14): 3236-3244
DF	Früh, K. et al. (1995) "A Viral Inhibitor of Peptide Transporters for Antigen Presentation." <i>Nature</i> 375: 415-418
DG	Furth P. (1994) "Temporal Control of Gene Expression in Transgenic Mice By A Tetracycline-Responsive Promoter" <i>Proc. Natl. Acad. Sci. USA</i> 91:9302-9306
DH	Gatz et al. (1992) "Stringent repression and homogeneous de-repression by tetracycline of a modified CaMV 35S promoter in intact transgenic tobacco plants," <i>The Plant Journal</i> , 2(3):397-404
DI	Gatz, C. et al. (1991) "Regulation of a modified CaMV 35S Promoter by the Tn 10-encoder Tet repressor in Transgenic Tobacco" <i>Mol. Gen. Genet.</i> 227(2):229-237
DJ	Gatz, C. and P. Quail (1988) "Tn10-Encoded tet Repressor Can Regulate an Operator-Containing Plant Promoter" <i>Proc. Natl. Acad. Sci. USA</i> 85:1394-1397
DK	Gjetting, T. et al. (1995) "Regulated Expression of the Retinoblastoma Susceptibility Gene in Mammary Carcinoma Cells Restores Cyclin D1 Expression and G ₁ -Phase Control", <i>Biol. Chem. Hoppe-Seyler</i> , 376:441-446
DL	Gossen M. and B. Hermann (1993) "Anhydrotetracycline, A Novel Effector of Tetracycline Controlled Gene Expression Systems In Eukaryotic Cells" <i>Nucleic Acids Research</i> 21(18):4411-4412
DM	Gossen, M., et al. (1993) "Control of gene activity in higher eukaryotic cells by prokaryotic regulatory elements", <i>TIBS</i> 18(12):471-475
DN	Gossen et al. (1995) "Exploiting prokaryotic elements for the control of gene activity in higher eukaryotes," Keystone Symposium on Gene Therapy and Molecular Medicine, Steamboat Springs, Colorado, <i>Journal of Cellular Biochemistry</i> , Supplement 0 (21A), Abstract no. C6-220, 355
DO	Gossen et al. (1994) "Inducible Gene Expression Systems For Higher Eukaryotic Cells" <i>Current Opinion in Biotechnology</i> 5:516-520
DP	Gossen, M. and Bujard, H. (1992) "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters", <i>Proceedings of the National Academy of Science USA</i> 89:5547-5551
DQ	Gossen et al. (1995) "Transcriptional activation by tetracyclines in mammalian cells," <i>Science</i> , 268:5218, 1766-1769

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EA	Gunzburg, W.H. and Salmons, B. (1995) "Virus vector design in gene therapy", <i>Molecular Medicine Today</i> 1: 410-417
EB	Haase, S.B. et al. (1994) "Transcription Inhibits the Replication of Autonomously Replicating Plasmids in Human Cells", <i>Molecular and Cellular Biology</i> , 14(4):2516-2524
EC	Hammer, R.E. et al. (1986) "Genetic Engineering of Mammalian Embryos." <i>J. Anim. Sci.</i> 63: 269-278
ED	Hecht, B. et al. (1993) "Noninducible Tet Repressor Mutations Map from the Operator Motif to the C Terminus", <i>Journal of Bacteriology</i> 175(4):1206-1210
EE	Hennighausen, L. et al. (1995) "Conditional Gene Expression in Secretory Tissues and Skin of Transgenic Mice Using the MMTV-LTR and the Tetracycline Responsive System", <i>Journal of Cellular Biochemistry</i> , 59: 463-472
EF	Herschbach B. and A. Johnson (1993) "Transcriptional Repression In Eukaryotes" <i>Annu. Rev. Cell Biol.</i> 9:479-509
EG	Hillen, W. and Schollmeier, K. (1983) "Nucleotide sequence of the Tn10 encoded tetracycline resistance gene", <i>Nucleic Acids Research</i> 11(2):525-539
EH	Hinrichs, W. et al. (1994) "Structure of the Tet Repressor-Tetracycline Complex and Regulation of Antibiotic Resistance", <i>Science</i> 264:418-420
EI	Howe, J.R. et al. (1995) "The Responsiveness of a Tetracycline-Sensitive Expression System Differs in Different Cell Lines", <i>The Journal of Biological Chemistry</i> , 270, No. 23, pp. 14168-14174
EJ	Houdebine, L.-M. (1994) "Production of Pharmaceutical Proteins From Transgenic Animals", <i>Journal of Biotechnology</i> 34:269-287
EK	Hu, M.C-T and Davidson, N. (1987) "The Inducible <i>lac</i> Operator-Repressor System Is Functional in Mammalian Cells", <i>Cell</i> 46:555-566
EL	Kao, C.C. et al. (1990) "Cloning of a Transcriptionally Active Human TATA Binding Factor" <i>Science</i> 248: 1646-1650
EM	Kappel, C.A. et al. (1992) "Regulating Gene Expression In Transgenic Animals", <i>Current Opinion In Biotechnology</i> , 3:548-553
EN	Krimpenfort, P. et al. (1991) "Generation of Transgenic Dairy Cattle Using 'in vitro' Embryo Production." <i>BIO/Technology</i> 9:844-847
EO	Labow, M.A. et al. (1990) "Conversion of the <i>lac</i> Repressor into an Allosterically Regulated Transcriptional Activator for Mammalian Cells", <i>Molecular and Cellular Biology</i> 10(7):3343-3356
EP	Landschulz, W.H. et al. (1989) "The DNA Binding Domain of the Rat Liver Nuclear Protein C/EBP is Bipartite" <i>Science</i> 243: 1681-1688
EQ	Liang et al. (1995) "Enhanced and switchable expression systems for gene-transfer," Keystone Symposium on Gene Therapy and Molecular Medicine, Steamboat Springs, Colorado, <i>Journal of Cellular Biochemistry</i> , Supplement 0 (21A), Abstract no. C6-220, 379
ER	Licht, J. et al. (1990) "Drosophila Krüppel Protein is a Transcriptional Repressor" <i>Nature</i> 346:76-79
ES	Maheswaran, S. et al. (1995) "The WT1 Gene Product Stabilizes p53 and Inhibits p53-mediated Apoptosis." <i>Genes & Development</i> 9: 2143-2156

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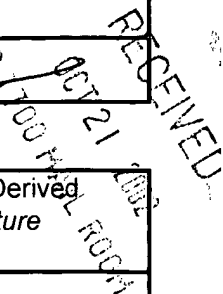
FA	Mansour, S.L. et al. (1988) "Disruption of the Proto-Oncogene <i>int-2</i> in Mouse Embryo-Derived Stem Cells: a General Strategy for Targeting Mutations to Non-Selectable Genes" <i>Nature</i> 336:348-352
FB	Marshall, E. (1995) "Gene Therapy's Growing Pains" <i>Science</i> 269: 1050-1055
FC	Mastrelangelo et al. (1996) "Gene Therapy for Human Cancer: An Essay for Clinicians" <i>Seminars in Oncology</i> 23 (1):4-21
FD	McKnight, S.L. (1984) "The Distal Transcription Signals of the Herpesvirus <i>tk</i> Gene Share a Common Hexanucleotide Control Sequence" <i>Cell</i> 37: 253-262
FE	Mendez, B. et al. (1980) "Heterogeneity of tetracycline resistance determinants" <i>Plasmid</i> 3:99-108
FF	Mermod N. et al. (1989) "The Proline-Rich Transcriptional Activator of CTF/NF-I Is Distinct from the Replication and DNA Binding Domain" <i>Cell</i> 58:741-753
FG	Miller, K. et al. (1995) "The Function of Inducible Promoter Systems in F9 Embryonal Carcinoma Cells", <i>Experimental Cell Research</i> , 218: 144-150
FH	Muller, G. et al. (1995) "Characterization Of Non-Inducible Tet Repressor Mutants Suggests Conformational Changes Necessary For Induction", <i>Nature Structural Biology</i> , 2 : 693-703
FI	Mullins, L.J. and Mullins, J.J. (1996) "Transgenesis in the Rat and Larger Mammals." <i>J. Clin. Invest.</i> 98(11) Supplement 1996: S37-S40
FJ	Murre, C. et al. (1989) "Interactions Between Heterologous Helix-Loop-Helix Proteins Generate Complexes That Bind Specifically to a Common DNA Sequence" <i>Cell</i> 58: 537-544
FK	Notarianni, et al. (1994) "Production of pharmaceutical proteins from transgenic animals", <i>Journal of Reproduction and Fertility</i> , 41: 51-56
FL	Orkin, S. H. and Motulsky, A.G. (1995) "Report and recommendations of the panel to assess the NIH investment in research on gene therapy" http://www.nih.gov/news/panelrep.html
FM	Passman, R.S. et al. (1994) "Regulated Expression of Foreign Genes In Vivo After Germline Transfer", <i>J. Clin. Invest.</i> , 94:2421-2425
FN	Pescini R. et al. (1994) "Inducible Inhibition of Eukaryotic Gene Expression" <i>Biochemical and Biophysical Research Communications</i> 202(3):1664-1667
FO	Postle, K. et al. (1984) "Nucleotide sequence of the repressor gene of the TN10 tetracycline resistance determinant", <i>Nucleic Acids Research</i> 12(12):4849-4863
FP	Pursel et al. (1989) "Genetic engineering of livestock" <i>Science</i> 244: 1281-1288
FQ	Renkawitz R. (1990) "Transcriptional Repression In Eukaryotes" <i>TIG</i> 6(6):192-193
FR	Resnitzky D. (1994) "Acceleration of the G1/S Phase Transition by Expression of Cyclins D1 and E with an Inducible System" <i>Molecular and Cellular Biology</i> 14(3):1669-1679
FS	Rubin, et al. (1990) "Interdomain hybrid Tet proteins confer tetracycline resistance only when they are derived from closely related members of the tet gene family." <i>J. Bacteriol.</i> 172:2303-12
FT	Salter, et al. (1987) "Transgenic chickens: insertion of retroviral genes into the chicken germ line" <i>Virology</i> 157: 236-240

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GA	Sato, K. et al. (1986) "A specific DNA Sequence Controls Termination of Transcription in the Gastrin Gene" <i>Molecular and Cellular Biology</i> 6(4): 1032-1043
GB	Sauer, F. and H. Jäckle (1993) "Dimerization and the Control of Transcription by Krüppel" <i>Nature</i> 364:454-457
GC	Seamark, R.F. (1994) "Progress and Emerging Problems in Livestock Transgenesis: a Summary Perspective." <i>Reprod. Fertil. Dev.</i> 6: 653-657
GD	Seipel, K., et al. (1992) "Different activation domains stimulate transcription from remote ('enhancer') and proximal ('promoter') positions", <i>The EMBO Journal</i> 11(13):4961-4968
GE	Shan, B., et al. (1994) "Deregulated Expression of E2F-1 Induces S-Phase Entry and Leads to Apoptosis." <i>Molecular and Cellular Biology</i> 14(12): 8166-8173
GF	Sizemore, C. et al. (1990) "Quantitative Analysis of Tn10 Tet Repressor Binding To A Complete Set Of Tet Operator Mutants", <i>Nucleic Acids Research</i> , 18(10): 2875-2880
GG	Smithies, O. et al. (1985) "Insertion of DNA sequences into the human chromosomal β -globin locus by homologous recombination", <i>Nature</i> 317:230-234
GH	Sopher, B.L. et al. (1994) "Cytotoxicity Mediated By Conditional Expression of a Carboxyl-Terminal Derivative of the β -Amyloid Precursor Protein", <i>Molecular Brain Research</i> , 26:207-217
GI	Strojek, et al. (1988) "The Use Of Transgenic Animal Techniques For Livestock Improvement", <i>Genetic Engineering, Principles and Methods</i> , 10: 221-246
GJ	Tovar, K. et al. (1988) "Identification and nucleotide sequence of the class E tet regulatory elements and operator and inducer binding of the encoded purified Tet repressor", <i>Mol. Gen. Genet.</i> 215:76-80
GK	Trizzenberg, S.J. et al. (1988) "Functional dissection of VP16, the trans-activator of herpes simplex virus immediate early gene expression", <i>Genes & Development</i> 2:718-729
GL	Unger, B. et al. (1984) "Nucleotide sequence of the gene, protein purification and characterization of the pSC101-encoded tetracycline resistance-gene-repressor", <i>Gene</i> . 31:103-108
GM	Unger, B. et al. (1984) "Nucleotide sequence of the repressor gene of the RA1 tetracycline resistance determinant: structural and functional comparison with three related Tet repressor genes", <i>Nucleic Acids Research</i> 12(20):7693-7703
GN	Wall, R.J. (1996) "Transgenic Livestock: Progress and Prospects For The Future" <i>Theriogenology</i> , 45: 57-68
GO	Waters, S.H. et al. (1983) "The tetracycline resistance determinants of RP1 and Tn1721: nucleotide sequence analysis", <i>Nucleic Acids Research</i> 11(17):6089-6105
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